Investigation into the Effects of Hydrodynamic Shear Stress on Nanoparticle-Cell Interactions

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While there have been significant advances in the fields of nanotoxicology and nanomedicine in the past decade, there have been relatively few successes translating nanomedicines into the clinic and there still exist significant gaps in our understanding of the phenomena governing nanoparticle-mediated cellular effects (*e.g.* cytotoxicity).[1,2] In an effort to better understand the fundamental interactions of nanoparticles (NP) with biological systems, some researchers are turning towards more complex *in vitro* systems. Microfluidics are particularly relevant because they enable the study of NP under hydrodynamic (flow) conditions, a most likely scenario for any systemically administered nanomedicines or NP which are able to enter the blood stream.[3,4] In the presented work, we investigated the effects of hydrodynamic shear forces on NP-cell interactions.

Rhodamine B-labelled silica NP with a diameter of 60 nm (SiNP) were used as a model NP, and a custom built microfluidic cell system[5] was used to study the uptake of SiNP by J774A.1 mouse monocyte/macrophages. J774A.1 were arrested in the flow chamber under low shear stress conditions (0.1 dyn/cm^2) on a recombinant intercellular adhesion molecule 1 (rICAM-1)-treated surface or on top of a monolayer of primary mouse lung endothelial cells (pMLEC) treated with tumor necrosis factor alpha (TNFα). Cells were then exposed to SiNP under either static conditions or flow at 1.5 dyn/cm^2. Association of SiNP with J774A.1 cells was assessed by measuring fluorescent intensity of individual cells within regions of interest (ROI) over the course of the NP exposure. Preliminary data showed that more NPs were internalized by cells at the end of the exposure under flow conditions, in addition to exhibiting a higher NP uptake rate. Furthermore, observation of J774A.1 arrested on the pMLEC showed events of macrophage diapedesis, and transport of the internalized SiNP through the endothelial cell monolayer.

The preliminary data has significant implications, as static NP-cell interaction studies may not adequately describe the complex physiological environment NP face in the body. Moreover, this system has potential to be expanded to study other important biological phenomena (*e.g.* transport of NP across biological barriers).

References

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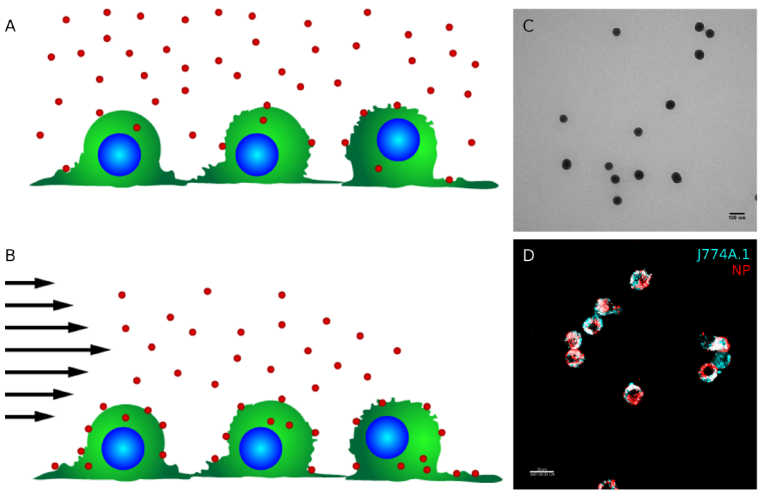

Schematic representation of SiNP uptake by macrophages under (A) static and (B) flow conditions. (C) Transmission electron microscopy images showing SiNP with a diameter of 60 nm. Scale bar represents 100 nm. (D) Live cell confocal laser scanning microscopy of J774A.1 uptaking SiNP under static conditions after 1 hr of exposure. Scale bar represents 20 µm.